REMARKS

Claims 23-44 are pending. Applicants elect with traverse Group I (claims 23-28, 33-39 and 44) for examination on the merits. In response to the new requirement for an election of species, Applicants elect fusion protein PjEDcys (SEQ ID NO:4): a heterodimer comprising Parj1 and Parj2. Each subunit of the heterodimer has four disulphide bridges, in the order: 4-52, 14-29, 30-75 and 50-91. In the elected species, the first three disulphide bridges are missing and the last disulphide bridge (Cys50-Cys91) is present. No residue is eliminated as compared to the wild type sequences of Parj1 and Parj2. Cysteine at positions 4, 29 and 30 in each of Parj1 and Parj2 are replaced by serine, respectively. Claims 23-28, 33-39 and 44 read on the elected species.

Applicants reserve the right to prosecute nonelected subject matter in a further patent application.

Notwithstanding the above election, reconsideration of the restriction requirement is requested because examination of all pending claims would not constitute a serious burden. Although the inventions identified by the Examiner are separately patentable, both the need for compact prosecution and the public interest would be served by examination of all claims in a single application. In particular, the claims of both Groups I and II should be examined in the same application. Thus, claims 29-32 and 40-43 should not be withdrawn from consideration.

Applicants disagree with the Examiner's restriction requirement because there is unity of invention. In particular, the claims are novel and nonobvious as shown by the unexpected effects obtained by the claimed fusion protein, which is a special technical feature shared by the pending claims. The experimental results discussed in the last paragraph of page 6 (lines 26-37) and first paragraph of page 7 (lines 1-18) of the specification support the patentability of the claimed fusion protein. Those results are summarized below for elected and nonelected species.

Fusion protein PjEDcys (SEQ ID NO:4) has a very low capability of interacting with IgE as shown in the specification (see Fig. 5). Its binding percentage in different patients was only 7%, 3.5%, 10% or 8% respectively. The ability to interact with IgE (% of IgE binding inhibition) is markedly lower than that of heterodimer Parj1-Parj2 wild

type (line "Dimer W.T." in Fig 5: 56%, 68% or 62%); individual modified allergens PjA, PjB, PjC and PjD all showing binding inhibition of 14% or higher (Fig. 9); or recombinant wild type Parj1 or Parj2 or a mixture thereof (Fig. 8). This reduced allergenicity was also accompanied by an unaltered, or even enhanced, immunogenicity as demonstrated by Fig. 7 (panels B and C and the bottom table).

Nonelected species, now excluded from consideration by the Examiner's new requirement, show the same unexpected properties, which directly derive from fusion of two ns-LTP allergens lacking one or more disulphide bridges.

Fig. 9 shows that PjA, PjB, PjC and PjD all exhibit a decreased binding capability for IgE as compared to recombinant wild type Parj1. They were previously described in WO 02/20790 and represent modified forms of ParJ1: (a) Cys residues at positions 29 and 30 in PjA are replaced by a Ser residue (i.e., lacking disulphide bridges 14-29 and 30-75); (b) Cys50 and Cys52 in PjB are replaced by two Ser residues (i.e., lacking disulphide bridges 4-52 and 50-91); and (c) Cys4, Cys29 and Cys30 in PjC are replaced by three Ser residues (i.e., lacking disulphide bridges 4-52, 14-29 and 30-75). On the one hand, Fig. 9 shows that any modification reducing the number of disulphide bridges brings about a decreased capability of binding the IgE (involved in all allergic events). On the other hand, Fig. 5 shows that the heterodimer of modified allergens exhibits a strongly decreased capability for binding to IgE as compared to the corresponding heterodimer of Parj1 and Parj2 wild type.

From the above, one of skill in the art would reasonably expect that <u>any</u> fused protein comprising ParJ1 and ParJ2 allergens lacking one or more disulphide bridges would have a decreased capability of raising an allergic reaction as compared to that of PjEDcys. For this reason, all of the fused proteins belonging to the elected invention are patentable and have unity of invention.

Finally, in accordance with the Commissioner's Notice of March 26, 1996 (1184 OG 86) implementing the Federal Circuit's decisions of *In re Ochiai*, 37 USPQ2d 1127 (1995) and *In re Brouwer*, 37 USPQ2d 1663 (1996), Applicants request <u>rejoinder</u> of nonelected method claims upon an indication that an elected product claim is allowable.

Applicants earnestly solicit an early and favorable examination on the merits. The Examiner is invited to contact the undersigned if additional information is required.

Respectfully submitted,

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